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(54) Title of the Invention

Method for Purifying an Albumin-Containing Aqueous Solution

[Claims]

[Claim 1] A method for purifying an albumin-containing aqueous solution characterised in that an albumin-containing aqueous solution originated from serum and contaminated with aluminium is subjected to a treatment with a strong anion exchanger to remove the contaminating aluminium.

[Claim 2] A method for purifying an albumin-containing aqueous solution according to Claim 1 wherein the aluminium content in the albumin-containing aqueous solution originated from serum and obtained by treating with a strong anion exchanger is 70 ppb or less.

[Detailed Description of the Invention]

[Field of Application]

This invention relates to a method for purifying an albumin-containing aqueous solution and, more particularly, it relates to a method for reducing the aluminium content in an albumin-containing aqueous solution useful as a starting material for albumin preparations.

Further, the relationship between aluminium in brain and Alzheimer's disease (senile dementia) has attracted attention.

For this reason, various attempts have been made in European countries and the USA to control the aluminium content in medical preparations.

This invention aims at solving the above problems and its purpose is to provide a method for considerably reducing the aluminium content of an albumin-containing aqueous solution comprising aluminium.

[Means for Solving the Problems]

The authors of this invention carrier out intensive research in order to reduce the aluminium content in an albumin preparation. As a result, they have found that the aluminium content of an albumin-containing aqueous solution comprising aluminium can be reduced by a treatment with an anion exchanger. The present invention is based on the above findings. Namely, the invention is a method for purifying an albumin-containing aqueous solution wherein an albumin-containing aqueous solution originated from serum (serum albumin) and contaminated with aluminium is subjected to a treatment with an anion exchanger to remove the contaminating aluminium. After performing a treatment with cation exchanger and a heat treatment, the purified albumin-containing aqueous solution can be formulated into an albumin preparation.

Hereinafter, the invention is explained in detail.

ering the efficiency for eliminating aluminium, it is preferable to use strong anion exchangers, such as Q-Sepharose and QAE-Toyopearl.

The treatment with the said anion exchanger may be performed by contacting the albumin-containing aqueous solution with the anion exchanger. The amount of the anion exchanger may be selected in function of the aluminium content in the albumin-containing aqueous solution, the amount of contaminating proteins and the exchanging capacity of the anion exchanger, but, per 1 g of albumin, from 2 to 5 ml, usually about 3 ml of the anion exchanger may be used. This treatment may be performed either by the column method or by the batch method, but the column method is preferable from the viewpoint of the efficiency of eliminating aluminium.

In the case of the column method, the above-mentioned albumin-containing aqueous solution is adjusted to pH from 3 to 6, preferably from 4.5 to 5.5, and to a salt concentration of from 0.001 to 0.2M, preferably from 0.001 to 0.05M, in terms of sodium chloride and passed through an anion exchange column equilibrated with a buffer solution [for example, 0.02M sodium acetate buffer (pH 5.1)]. Then, the column is developed with the same buffer solution to recover the unadsorbed material. This procedure is performed at a low temperature (usually, 10°C or below) to prevent the denaturation of albumin.

In the case of the batch method, the anion exchanger is added to the albumin-containing aqueous solution which has

aqueous solution, the exchanging capacity, etc. of the cation exchanger. In general, for 1 g albumin, from 2 to 5 ml, usually about 2 ml, of cation exchanger is used. The treatment may be performed either by the column method or by the batch method. The column method is preferred considering the efficiency of eliminating contaminating proteins.

In the case of the column method, the above-mentioned albumin-containing aqueous solution is adjusted to pH from 4 to 8, preferably from 4.5 to 6.0, still more preferably 5.5, and to a salt concentration of from 0.001 to 0.2M, preferably from 0.001 to 0.05M, in terms of sodium chloride and passed through a cation exchange column equilibrated with a buffer solution [for example, 0.02M sodium acetate buffer (pH 5.1)]. Then, the column is developed with the same buffer solution to recover the unadsorbed material. This procedure is performed at a low temperature (usually, 10°C or below) in order to prevent the denaturation of albumin.

In the case of the batch method, the cation exchanger is contacted with to the albumin-containing aqueous solution prepared under the above-mentioned conditions. After mixing at 10°C or below for 30 minutes to 2 hours, the solution is separated from the cation exchanger by centrifugation or other means and the supernatant is recovered.

In the next step, the albumin-containing aqueous solution with aluminium content and contaminating protein content reduced by the said treatments with the anion exchanger and the

[Examples of Embodiment]

In the following, an Example of Embodiment and Experimental Example are given to further illustrate the present invention in greater detail. But the invention is not limited by this Example of Embodiment.

Example of Embodiment

(1) Preparation of Albumin-containing Aqueous Solution

A paste of the fraction V (500 g) obtained by Cohn's cold alcohol fractionation was dissolved in 2.0 litre of cold sterile distilled water, the pH value of the solution was adjusted to 4.6 with acetic acid and the solution was stirred for about 1 hour. Then, it was filtered (filter: 0.45 μm) at about –2°C through a filter filled with a filtering additive. Again, 2.0 litre of cold sterile distilled water was added and the pH value of the mixture was adjusted to 5.1 with 1N sodium hydroxide to obtain an albumin-containing aqueous solution.

(2) Treatment with Anion Exchanger

QAE-Toyopearl (580 ml) was packed into a column (diameter 5 cm x height 18 cm) and thoroughly washed with 0.5M sodium chloride. After equilibration with 0.02M sodium acetate (pH 5.1), an anion exchange column was obtained. Then the albumin-containing aqueous solution obtained in the above (1) was passed over the column and the column was washed further with cold 0.02M sodium acetate (pH 5.1, 2 litre). The effluent and the washing liquid were combined and the pH value of

Experimental Example

In view of evaluating the effect of a treatment with an anion exchanger, the efficiency of aluminium removal was compared in a system without treatment with anion exchanger (non-treated system), a system with weak anion exchanger treatment (DEAE treated system) and a system with strong anion exchanger treatment (QAE treated system). Conditions other than those concerning the treatment with anion exchanger were the same as described in the Example of Embodiment. The aluminium content of the albumin preparation obtained was determined by atomic absorption spectrometry. The results are shown in Table 1.

Table 1 shows that the aluminium content can be reduced by a treatment with anion exchanger and the extent of reduction is particularly elevated in the case of treating with a strong anion exchanger.

Table 1

	Aluminium content (ppb)
Non-treated system	1250
DEAE treated system	480
QAE treated system	70